Hormone Replacement Therapy as Adjuvant Treatment of Epithelial Ovarian Cancer?

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"Does a face need words?
¿Does the flower want sounds?
Do the dog, stone, fire
Ask for nouns?
Don’t they express themselves just by being?"


Cancer treatment sometimes can have a decisive impact on the reproductive function in women. The eventual ovarian failure generated by surgery, chemotherapy and/or radiotherapy makes necessary to arise under a very stringent criterion the hormone replacement therapy (HRT) in order to alleviate symptoms and prevent sequelae resulting from hormonal deprivation. There are some types of cancer that are absolute contraindications for its use, such as hormone-dependent neoplasms, like breast or endometrial cancer, in which case it is necessary to prevent the effects of the lack of estrogen on its target organs with non-hormonal therapies.

The modern conception of cancer treatment aims to eradicate the disease within a framework of security without involving other organs than the affected by neoplasia. In cases in which the ovary is involved, treatment cancels its endocrine and reproductive function with important effects especially on young women. It is well known that the hypoestrogenism at an early age is associated with degenerative diseases such as osteoporosis, senile dementia, Parkinson’s disease,
cardiovascular diseases or gynecological and genitourinary disorders that compromise the quality of life of the patients. Women with premature ovarian failure are ostensibly at risk of morbidity and mortality of different causes than the patients who maintain the ovarian function up to the average age of menopause.

There are some types of non-hormone-dependent cancer on which the safety of HRT has not been determined, and has even considered that previous use of this therapy could increase this risk, as is the case of ovarian cancer, aspect that we have already mentioned in a former article, which evaluates a meta-analysis published in February 2015 in *The Lancet* where it was observed an increase in the risk of ovarian cancer in HRT users.

In September 2015, is published in the *Journal of Clinical Oncology* the largest series of patients with ovarian cancer in treatment with HRT until the date. A multicenter, randomized, controlled clinical study evaluated the use of TRH in patients with ovarian cancer after oncologic treatment. It was included 150 patients, half of them assigned to sample group who would receive HRT and the other half to the group that would not get it. Of the 75 patients assigned to the treatment group, 72 patients received at least one dose of HRT with an average of 1.14 years of HRT use. HTR types used by the patients were: conjugated equine estrogens with and without norgestrel, and patch and implant estradiol. Treatment with HRT was fully met by 26 patients until the last control or death; the other 46 suspended treatment for various reasons: side effects, recurrence of neoplasia, second primary, etc.

After 19 years of follow-up the results are interesting: overall survival was 37% higher in patients receiving HRT than in those that did not (HR: 0.63; p 0.011), which rises to 55% after adjusting for menopausal status, FIGO stage and prognostic factors (HR: 0.45, p 0.001). A total of 122 patients evaluated had relapse or death by any cause: 72% in the group receiving HRT and 91% in the control group, for which relapse-free survival was also higher in the group that received HRT: 28% vs 9% (HR: 0.67, p: 0.032), with an improvement when adjusting for prognostic factors (HR: 0.53, p: 0.004). Despite the long period of follow-up, the limited number of patients who fulfilled the HRT for five years, the recommendation of the authors is to use HRT in epithelial ovarian cancer given the positive impact on the quality of life and survival should be advised.

Since epithelial ovarian cancer is not considered in the accepted carcinogenetic models an estrogen-dependent neoplasm there would not be a formal contraindication for the use of HRT after this pathology. According to the results presented, at least one year of HRT improves not only the quality of life for these patients, but the overall and relapse-free survival, which requires further research to determine its true value as part of the treatment of this pathology.

The question that arises is: what is the mechanism through which the HRT would improve the survival of these patients? Overall survival may increase due the decrease in the incidence of other pathologies generated by premature ovarian failure. The pathophysiological mechanism that would explain the decrease in relapses by cancer of ovary with the use of estrogen is maintained in a speculative field. However it could be explained through the effect of pituitary follicle stimulating hormone (FSH), as a suppressor of apoptosis in the ovary and stimulator of the synthesis of the
VEGF (vascular endothelial growth Factor). When decrease the estrogen plasma level, occurs a sustained increase in FSH level which could affect the neoplastic cells, stimulating its growth and favouring the neoangiogenesis through the VEGF. On the contrary, the use of estrogen in patients treated for epithelial ovarian cancer, would keep FSH low, avoiding its promoting effect on neoplastic cells. This mechanism also explains why oral contraceptives, which are also suppress the pituitary FSH have shown a preventive effect against this neoplasia.

Although it is still premature to anticipate a definitive conclusion, these influential study results allow to predict that prescribe HRT in patients with epithelial ovarian cancer could be, in the short term, a formal indication of the use of this treatment to ensure quality of life and increase survival in these patients. If the evidence presented is finally confirmed HRT could be considered, in the near future, as the first adjuvant endocrine treatment of epithelial ovarian cancer.

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